

## METHODS

## MD1

**A TALE OF TWO STUDIES: A COMPARISON OF ECONOMIC DATA FROM A CLINICAL TRIAL TO A CROSS-SECTIONAL DATABASE**

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When economic evaluations are conducted alongside clinical trials estimates of resource utilization (RU) are likely to be inaccurate. This problem arises due to presence of protocol-mandated visits and forced compliance. It is rare to find two databases that may be compared to determine the scale of this problem. **OBJECTIVE:** 1) To compare the resource utilization associated with rheumatoid arthritis from a clinical trial database to a cross-sectional database, and 2) to understand advantages and disadvantages of using each database in economic analyses. **METHODS:** In this novel study, two databases were examined: one a pragmatic, cross-sectional database (CSD: with 6-month retrospective recall of RU) of rheumatoid arthritis patients (RA) and the other a database from a phase III clinical trial program (CTD) in RA matched on several demographic variables. Subjects were age/gender matched to control for differences in the database populations. Hospitalizations, GP and specialist visits were compared between the databases. **RESULTS:** When the CTD is examined for just protocol visits, a total of 8 specialist consultations were recorded. When the CTD is examined for non-protocol visits, few additional visits are recorded: 0.12 GP visits, 0.11 specialist consultations, and 0.01 hospitalizations. The addition of the non-protocol visits to the protocol total visits increase RU to 8.12 GP visits and 8.11 specialist consultations. Based on data from the CSD, over a 6-month time frame, randomly matched on age and gender, an average of 2.1 GP visits, 2.21 specialist consultations, and 1.3 hospitalizations were reported by patients. **CONCLUSIONS:** The inclusion of protocol-mandated visits substantially overstates true RU while their omission understates thereby leaving researchers in a quandary. The use of CTDs for modeling purposes raises the issues of generalizability and accuracy and suggests that naturalistic rather than piggyback trials should be used for PE evaluations.

## MD2

**THE PARAMETRIC BOOTSTRAP: RECONCILING PARAMETRIC AND NON PARAMETRIC METHODS IN THE ESTIMATION OF CONFIDENCE INTERVALS FOR INCREMENTAL COST-EFFECTIVENESS RATIOS?**

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**OBJECTIVES:** Many authors have addressed the issue of handling uncertainty in stochastic cost-effectiveness

analyses. They generally oppose parametric (Fieller's theorem, confidence box or ellipse ...) and non parametric (bootstrap) methods. The parametric bootstrap is at the bridge of these two families of methods. Parametric bootstrap was used to assess confidence interval of the incremental cost-effectiveness ratio (ICER) of a drug used in the treatment of post-infarction patients and the estimated CI was compared to that provided by non parametric bootstrap. **METHODS:** Data were derived from a placebo-controlled clinical trial on 1749 patients included just after MI and followed over 4 years. Patient-level costs were computed to reflect the US Health care system. The parametric bootstrap was based on the assumption that the incremental costs and effects differentials follow a normal bivariate distribution. Five thousand re-samples were made from the normal bivariate density function. The non parametric bootstrap was based on 5000 re-samples from the original sample. Mean ICER estimates and percentiles CI are presented for both techniques. **RESULTS:** The mean ICER from the original sample was estimated to US\$2574 per life-year saved. The parametric bootstrap provided an estimated ICER of US\$2726/LYS and the 95% CI was [1164; 5210]. From the non parametric bootstrap, the ICER estimate was US\$3419/LYS and the 95% CI was [1660; 5254]. **CONCLUSIONS:** The parametric bootstrap provided a CI, which seemed to be in accordance with that of the non parametric bootstrap. It still needs to be compared to other parametric and non parametric methods, particularly in terms of coverage properties. It can be a useful tool, as it allows assumptions on the ICER joint distribution, without implying specific textbook formulae.

## MD3

**THE IMPLICATIONS OF COMBINING HETEROGENEOUS PATIENT POPULATIONS IN META-ANALYSES**

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Systematic reviews and meta-analyses attempt to minimise the biases from individual trials but can, on some occasions, miss or conceal beneficial treatment effects when trials, with varying patient populations, are analysed together. **OBJECTIVE:** To investigate the effect of 'splitting' diverse patient populations using part of a published meta-analysis of randomised controlled trials for the prevention of vascular events in high-risk patients. **METHODS:** Our study re-evaluated a section of results of a well-known meta-analysis of RCTs for the prevention of vascular events. The original review (ATC) estimated the combined treatment effect of dipyridamole plus aspirin (DP + ASA) compared to aspirin (ASA) alone using data from 25 clinical trials for all patients, regardless of their vascular morbidity profile. Patients who had previously experienced an MI, TIA/stroke, CABG, coronary angioplasty, intermittent claudication, peripheral